REMARKS

The Invention

In general, the presently claimed invention features methods for altering gene expression of a cell by incubating a nucleus or a chromatin mass from a donor cell with a reprogramming media under conditions that allow the addition or removal of a factor, and then inserting the nucleus or chromatin mass into a recipient somatic cell.

The Office action

Claims 1-31 are pending. Claims 3, 10-13, 17, and 24-30 are withdrawn from consideration as being drawn to nonelected subject matter. Claims 1, 2, 4-9, 14-16, 18-23, and 31 stand rejected as lacking enablement. Claims 1, 2, 14-16, and 18-23 stand further rejected as being supported by an inadequate written description. Claim 4 stands further rejected as being indefinite. Claims 1, 4-9, 21-23, and 31 stand rejected as being anticipated by DiBerardino et al., (Proc. Natl. Acad. Sci. USA 83:8231-8234, 1986), Schnieke et al., (Science 278:2130-2133, 1997), Sun et al. (Cancer Gene Ther. 5:110-118, 1998), Li et al. (Eur. J. Biochem. 262:211-217, 1999), Anderson et al. (U.S. Patent No. 5,654,183), de Anta (Histol. Histopathol. 12:33-41, 1997) and/or Risau et al. (Development 102:471-478, 1988). Each of these rejections is addressed in detail below.

Support for amendments

As amended, claims 1 and 2 are now directed to method of altering gene expression. Support for this amendment is found throughout the specification (see, e.g., page 27, line 27, and page 63, line 18). Claims 1 and 2 have further been amended to recite that the recipient cell is a somatic cell. Support for this amendment is found at page 66, line 12. Support for new claims 32-49 is found throughout the specitfication.

Rejections under 35 U.S.C. § 112, first paragraph

Written Description

Claims 1, 2, 14-16, and 18-23 are rejected as failing to comply with the written description requirement. The Office contends that "[t]he specification fails to provide adequate written description for what factors would be removed from a donor nucleus or added from the reprogramming media." Applicants respectfully traverse this rejection.

Claims 1 and 2, the sole independent claims under consideration by the Office, are directed to methods that include a step of incubating a nucleus (claim 1) or a chromatin mass (claim 2) from a donor cell with a reprogramming media under conditions that allow the addition or removal of a factor. Contrary to the Office's position, in order to practice the invention, one skilled in the art need not know what factors would be added or removed during the incubation of the nucleus or chromatin mass. Rather, what is important is that a factor be added or removed during the incubation. In one example, a B-cell nucleus is incubated in a skeletal muscle cell extract under conditions that allow for the removal of a factor from the B-cell nucleus and/or addition of a factor from the skeletal muscle cell extract to this nucleus. The incubated nucleus is then inserted into a recipient cell.

The significance of the recitation of the addition or removal of a factor from the incubated nucleus or chromatin mass is to define the conditions under which the nucleus or chromatin mass is incubated; if the conditions do not permit addition or removal of a factor, then the method would not be covered by the claim. One in the art would not require knowledge of the factors to be added or removed in order to ascertain whether suitable conditions are present. Because the identity of any added or removed factor is not "essential or critical" (as alleged by the Office), applicants submit that the rejection of claims 1 and 2 (and claims dependent therefrom) as lacking an adequate written description should be withdrawn.

Enablement

Claims 1, 2, 4-9, 14-16, 18-23, and 31 are rejected for lack of enablement. According to the Office, the claims are not enabled because "the specification fails to show that the cells...are indeed converted into a desired cell type, i.e., reprogrammed. The showing of increase or decrease of protein or gene expression fails to show that the cells are a different type of cell." The Office further argues that reprogramming is unpredictable, and cites three scientific papers -- Kikyo et al., Gurdon et al., and Wade et al. -- in support of this position.

As an initial matter, applicants respectfully disagree with the Office's contention that reprogramming requires an absolute alteration in cell type. The instant application is replete with examples in which, following the exposure of the donor cell nucleus with a reprogramming media, gene expression was significantly altered but endogenous gene expression of the donor nucleus was not entirely eliminated. In applicants' view, such altered gene expression is a reprogramming -- the gene expression profile of the "reprogrammed" cell is different from that of a cell not exposed to the reprogramming media.

Nonetheless, to clarify the distinction between applicants' usage of the word "reprogrammed" and that of the Office, applicants have amended the claims to recite methods of "altering gene expression." The Office acknowledges that applicants have enabled such methods, as is appropriate, given, for example, applicants' description of working examples at pages 49-63 of the specification. Applicants submit that, in view of the present amendment of claims 1 and 2 and the foregoing remarks, the rejection of the claims for lack of enablement may be withdrawn.

Applicants further note that the claims have been amended to specify that the recipient cell is a somatic cell. In view of this amendment, applicants submit that the three references relied upon by the Office as supporting its position that "reprogramming" is unpredictable are not relevant to the pending claims. This is because each of these three references summarizes the use of reprogramming in the field of cloning, an entirely different endeavor from that described in the present application. In

nuclear transfer-mediated cloning, the subject of the cited references, a somatic cell nucleus is transplanted into an enucleated oocyte, with the hope that the oocyte cytoplasm will reprogram the nucleus and permit development of an entire cloned animal. Clearly, in order to create a normal, cloned animal, the reprogramming described by the prior art references must be fairly complete; otherwise developmental issues may arise. The claimed reprogramming method of the present application does not include the use of oocytes -- the claims require that the recipient cell be a somatic cell -- and production of a cell that is not fully converted to a new cell type is nonetheless useful. Indeed, the specification states at page 2, line 15, that the production of cells possessing the characteristics of multiple cell types may be desirable.

Because the extent of cell type conversion required in the claimed method is entirely different from that necessary in the field of animal cloning, the concerns brought forth by the authors of the cited papers regarding the unpredictability of reprogramming are simply not relevant to the present invention. Accordingly, these papers do not support a position that it would require undue experimentation to practice the claimed methods.

Rejections under 35 U.S.C. § 112, second paragraph

Claim 4 is rejected as being indefinite. Claim 4 has been cancelled, and this rejection is now moot.

Rejections under 35 U.S.C. § 102

Claims 1 and 21-23

Claims 1, 21, and 22 are rejected as being anticipated by DiBerardino, while claims 1 and 21-23 are rejected as being anticipated by Schnieke. As applied to amended claim 1, this rejection may be withdrawn.

Amended claim 1 is directed to a method of reprogramming a cell by (a) incubating a nucleus from a donor cell with a reprogramming media and (b) inserting the

nucleus (or a chromatin mass formed from the nucleus) into a recipient somatic cell or cytoplast. As amended, the claim now specifies that the recipient cell is a somatic cell.

Transfer of a nucleus from one cell into a recipient somatic cell is neither taught nor suggested by either DiBerardino or Schnieke. In each of the cited references, the recipient cells are oocytes, not somatic cells. Accordingly, rejection of claim 1 (and claims dependent therefrom) as being anticipated may now be withdrawn.

Claims 4-9 and 31

Claims 4-9 and 31 are rejected as being anticipated by Sun, Li, Anderson, de Anta, and/or Risau. Applicants have cancelled these claims, and these rejections may now be withdrawn. Applicants reserve the right to pursue these claims in this or a related application.

CONCLUSION

Applicants submit that the claims are now in condition for allowance, and such action is respectfully requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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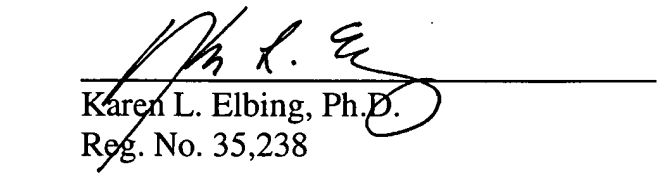

Karen L. Elbing, Ph.D.
Reg. No. 35,238

Clark & Elbing LLP
101 Federal Street
Boston, MA 02110
Telephone: 617-428-0200
Facsimile: 617-428-7045